## **WHAT IS CLAIMED IS:**

1	1. A compound that binds to a cysteine residue in the RNA-dependent
2	RNA polymerase (RdRp) protein of a virus forming a covalent bond.
1	2. A compound of Claim 1, wherein said RdRp protein is NS5B.
1	3. A compound of Claim 1, wherein said virus is hepatitis C virus
2	(HCV).
1	4. A compound of Claim 1, wherein said cysteine residue corresponds
1	/ /
2	to cysteine 366 in HCV NS5B.
3	5. A compound of Claim 1, wherein said RdRp is NS5B and said
4	virus is HCV.
7	// //
1	6. A compound of claim 5, wherein said covalent bond is irreversible
2	under physiological conditions.
1	7. A compound of claim 5, wherein said covalent bond is reversible
2	under physiological conditions.
1	8. A compound of claim 1, wherein said covalent bond results from a
2	reaction selected from the group consisting of a Michael addition of said cysteine residue
3	to an activated double or triple bond in said compound, an aromatic or aliphatic
4	nucleophilic substitution reaction of said cysteine residue with an electrophilic center in
5	said compound, a thioester forming reaction between said cysteine residue and a
6	carboxylic acid or carboxylic acid derivative in said compound, a disulfide forming
7	reaction between said cysteine residue and a sulfur-containing group in said compound,
8	and a hemi-thioketal forming reaction between said cysteine residue and an activated or
9	unactivated carbonyl group in said compound.
1	9. A compound useful for the covalent modification of a viral RNA-

- dependent RNA polymerase (RdRp) protein, said compound having the formula (I): 2  $X^{1}-L^{1}-X^{2}-A-L^{2}-Ar^{1}$
- 3
- wherein 4

5	A is a electrophilic group that reacts with a cysteine residue of said RdRp
6	protein;
7	Ar <sup>1</sup> is a member selected from the group consisting of substituted or
8	unsubstituted aryl and substituted or unsubstituted heteroaryl;
9	X1 is a member selected from the group consisting of -H, substituted or
10	unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted
11	heteroaryl, -CN, -CO <sub>2</sub> H, -SO <sub>3</sub> H, -C(O)NHOH, -NH <sub>2</sub> , -OH, -NH(lower alkyl), -O(lower
12	alkyl), $-N(lower alkyl)_2$ , and $-C(O)-NH(3-tetrazolyl)$ ;
13	L <sup>1</sup> is a divalent linking group selected from the group consisting of
14	$-CH_2CH_2-, -CH=CH-, -C\equiv C-, -O-, -S(O)_n-, -N(R_a)-, -C(O)-, -C(O)O-, -SO_2N(R_a)-, -C(O)-, -C(O)O-, -SO_2N(R_a)-, -C(O)-, -C(O)O-, -SO_2N(R_a)-, -C(O)O-, -C(O)O-, -SO_2N(R_a)-, -C(O)O-, -C(O)O-, -C(O)O-, -SO_2N(R_a)-, -C(O)O-, -C(O)O$
15	$-CON(R_a)-, -N(R_a)CON(R_b)-, -N(R_a)N(R_b)-, -N(R_a)SO_2N(R_b)-, -N(R_a)SO_2-, -N(R_a)-O-, -N(R_a)SO_2-, -N(R_a$
16	=N-O-, lower alkylene, -O-lower alkylene, -S(O) <sub>n</sub> -lower alkylene, N(R <sub>a</sub> )-lower alkylene
17	$-SO_2N(R_a)$ -lower alkylene, lower alkylene- $SO_2N(R_a)$ -, $-CON(R_a)$ -lower alkylene, lower
18	alkylene- $CON(R_a)$ -, $-N(R_a)CON(R_b)$ -lower alkylene, lower alkylene- $N(R_a)N(R_b)$ -,
19	$-N(R_a)SO_2N(R_b)$ -lower alkylene, $-N(R_a)$ -O-lower alkylene, lower alkylene- $N(R_a)$ -O-,
20	=N-O-lower alkylene, lower heteroalkylene, -O-lower heteroalkylene, -S(O) <sub>n</sub> -lower
21	heteroalkylene, $N(R_a)$ -lower heteroalkylene, $-SO_2N(R_a)$ -lower heteroalkylene, lower
22	heteroalkylene-SO <sub>2</sub> N(R <sub>a</sub> )-, -CON(R <sub>a</sub> )-lower heteroalkylene, lower
23	heteroalkylene-CON(Ra)-, -N(Ra)CON(Rb)-lower heteroalkylene, lower
24	heteroalkylene- $N(R_a)N(R_b)$ -, - $N(R_a)SO_2N(R_b)$ -lower heteroalkylene, - $N(R_a)$ -O-lower
25	heteroalkylene, lower heteroalkylene-N(R <sub>a</sub> )-O-, =N-O-lower alkylene, aryl and
26	heteroaryl;
27	X <sup>2</sup> is a member selected from the group consisting of substituted or
28	unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted
29	cycloalkyl, and substituted or unsubstituted heterocycloalkyl;
30	L <sup>2</sup> is a divalent linking group selected from the group consisting of
31	$-CH_2CH_2-, -(C(R_c)=C(R_d))_m-, -O-, -S(O)_n-, -N(R_e)-, -C(O)-, -C(O)O-, -SO_2N(R_e)-,$
32	$-CON(R_e)$ -, $-N(R_e)CON(R_f)$ -, $-N(R_e)N(R_f)$ -, $-N(R_e)SO_2N(R_f)$ -, $-N(R_e)$ -O-, $=N$ -O-, lower
33	alkylene, perfluoro lower alkylene, polyfluoro lower alkylene, -O-lower alkylene,
34	-S(O) <sub>n</sub> -lower alkylene, N(R <sub>e</sub> )-lower alkylene, -SO <sub>2</sub> N(R <sub>e</sub> )-lower alkylene, lower
35	alkylene-SO <sub>2</sub> N(R <sub>e</sub> )-, -CON(R <sub>e</sub> )-lower alkylene, lower alkylene-CON(R <sub>e</sub> )-,
36	$-N(R_e)CON(R_f)-lower\ alkylene,\ lower\ alkylene-N(R_e)N(R_f)-,\ -N(R_e)SO_2N(R_f)-lower$
37	alkylene, -N(Re)-O-lower alkylene, lower alkylene-N(Re)-O-, =N-O-lower alkylene,

	38	lower heteroalkylene, -O-lower heteroalkylene, -S(O) <sub>n</sub> -lower heteroalkylene, N(R <sub>e</sub> )-lower
	39	heteroalkylene, $-SO_2N(R_e)$ -lower heteroalkylene, lower heteroalkylene- $SO_2N(R_e)$ -,
	40	-CON(Re)-lower heteroalkylene, lower heteroalkylene-CON(Re)-, -N(Re)CON(Rf)-lower
	41	heteroalkylene, lower heteroalkylene- $N(R_e)N(R_f)$ -, - $N(R_e)SO_2N(R_f)$ -lower
	42	heteroalkylene, $-N(R_e)$ -O-lower heteroalkylene, lower heteroalkylene- $N(R_e)$ -O-,
	43	=N-O-lower alkylene, aryl and heteroaryl, wherein $R_a$ , $R_b$ , $R_c$ , $R_d$ , $R_e$ and $R_f$ are each
	44	members independently selected from the group consisting of H, lower alkyl, lower
	45	heteroalkyl, -C(O)-lower alkyl, -C(O)-lower heteroalkyl, -S(O) $_2$ -lower alkyl, and -
	46	S(O) <sub>2</sub> -lower heteroalkyl;
	47	the subscript n is an integer of from 0 to 2;
	48	the subscript m is an integer of from 0 to 3;
	49	the bond between X <sup>2</sup> and A can be a single, double or triple bond,
	50	depending on the nature of $X^2$ and A; and
7	51	wherein when L <sup>1</sup> and L <sup>2</sup> may be linked together via a single bond, -O-, -S-
# #	52	or amide group to form a new 5 to 7 membered ring;
	53	with the proviso that when A is an $sp^2$ -hybridized carbon atom and $X^2$ is substituted or
the first that the time that the first	54	unsubstituted rhodanine, $L^1$ is not $-CH_2-CH_2-$ , $-CH=CH-$ , $-C\equiv C-$ or aryl.
	1	10. A compound in accordance with claim 9, wherein
=	2	X <sup>2</sup> is selected from the group consisting of a 5 to 7 membered cycloalkyl
	3	ring, a 5 to 7 membered heterocycloalkyl ring containing from 1 to 3 heteroatoms, an aryl
1	4	group and a heteroaryl group;
	5	A is selected from the group consisting of an sp <sup>2</sup> -hybridized carbon atom
	6	and an sp <sup>3</sup> -hybridized carbon atom;
	7	$L^2$ is a single bond; and
	8	$X^2$ and A are joined <i>via</i> a single or double bond.
	1	11. A compound in accordance with claim 10, wherein
	2	$X^2$ -A- is selected from the group consisting of:
		- · -

5

6

7

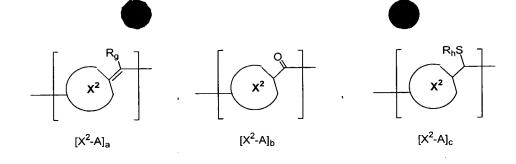
8

9

10

1

4 5



$$X^2$$
 and  $X^2$ -Al<sub>e</sub>  $X^2$ -Al<sub>e</sub>

 $[X^2-A]_d$   $[X^2-A]_d$ 

wherein  $R_g$  is selected from the group consisting of H, lower alkyl, lower alkoxy and F;  $R_h$  is selected from the group consisting of H,  $-S(O)_n$ -lower alkyl,  $-S(O)_n$ -lower heteroalkyl,  $-S(O)_n$ -aryl and  $-S(O)_n$ -heteroaryl;

W is CH or N; Hal is a halogen atom; and

 $X^2$  is a substituted or unsubstituted member selected from the group consisting of a 5-6 membered cycloalkyl, 5-6 membered heterocycloalkyl containing from 1 to 3 heteroatoms, heteroaryl containing from 1 to 3 heteroatoms and aryl.

12. A compound having the formula (II):

 $X^{1}-L^{1}-B-L^{2}-Ar^{1}$ 

3 wherein

Ar<sup>1</sup> is a member selected from the group consisting of substituted or unsubstituted aryl and substituted or unsubstituted heteroaryl;

X<sup>1</sup> is a member selected from the group consisting of -H, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, -CN, -CO<sub>2</sub>H, -SO<sub>3</sub>H, -C(O)NHOH, -NH<sub>2</sub>, -OH, -NH(lower alkyl), -O(lower alkyl), -N(lower alkyl)<sub>2</sub>, and -C(O)-NH(3-tetrazolyl);

10 L<sup>1</sup> is a divalent linking group selected from the group consisting of

 $11 \quad \text{-CH}_2\text{CH}_2\text{--, -CH} = \text{CH}_-, \text{-C} \equiv \text{C}_-, \text{-O}_-, \text{-S}(\text{O})_n\text{--, -N}(\text{R}_a)\text{--, -C}(\text{O})\text{--, -C}(\text{O})\text{O}_-, \text{-S}\text{O}_2\text{N}(\text{R}_a)\text{--, -S}(\text{O})_n\text{--, -N}(\text{R}_a)\text{--, -C}(\text{O})\text{--, -S}(\text{O})_n\text{--, -N}(\text{R}_a)\text{--, -C}(\text{O})\text{--, -S}(\text{O})_n\text{--, -N}(\text{R}_a)\text{--, -C}(\text{O})\text{--, -S}(\text{O})_n\text{--, -S}(\text{O})_n\text{--, -N}(\text{R}_a)\text{--, -C}(\text{O})_n\text{--, -S}(\text{O})_n\text{--, -S}(\text{O})_n\text{--,$ 

 $12 \quad -CON(R_a) -, \ -N(R_a)CON(R_b) -, \ -N(R_a)N(R_b) -, \ -N(R_a)SO_2N(R_b) -, \ -N(R_a)SO_2 -, \ -N(R_a) -O-, \ -N(R_a)SO_2 -, \ -N(R_a)S$ 

=N-O-, lower alkylene, -O-lower alkylene, -S(O)<sub>n</sub>-lower alkylene, N( $R_a$ )-lower alkylene,

 $-SO_2N(R_a)$ -lower alkylene, lower alkylene- $SO_2N(R_a)$ -,  $-CON(R_a)$ -lower alkylene, lower

alkylene- $CON(R_a)$ -,  $-N(R_a)CON(R_b)$ -lower alkylene, lower alkylene- $N(R_a)N(R_b)$ -,

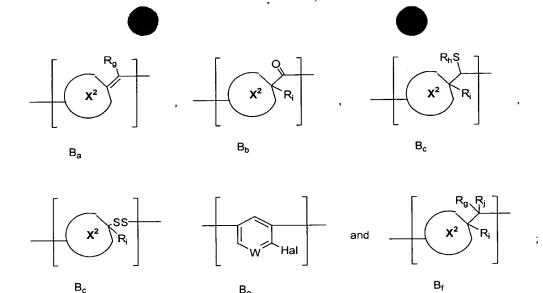
 $-N(R_a)SO_2N(R_b)$ -lower alkylene,  $-N(R_a)$ -O-lower alkylene, lower alkylene- $N(R_a)$ -O-,

43

	<u> </u>
17	=N-O-lower alkylene, lower heteroalkylene, -O-lower heteroalkylene, -S(O) <sub>n</sub> -lower
18	heteroalkylene, $N(R_a)$ -lower heteroalkylene, $-SO_2N(R_a)$ -lower heteroalkylene, lower
19	heteroalkylene-SO <sub>2</sub> N(R <sub>a</sub> )-, -CON(R <sub>a</sub> )-lower heteroalkylene, lower
20	heteroalkylene- $CON(R_a)$ -, $-N(R_a)CON(R_b)$ -lower heteroalkylene, lower
21	heteroalkylene- $N(R_a)N(R_b)$ -, - $N(R_a)SO_2N(R_b)$ -lower heteroalkylene, - $N(R_a)$ -O-lower
22	heteroalkylene, lower heteroalkylene-N(Ra)-O-, =N-O-lower alkylene, aryl and
23	heteroaryl;
24	L <sup>2</sup> is a divalent linking group selected from the group consisting of
25	$-CH_2CH_2-, -(C(R_c)=C(R_d))_{m^-}, -O-, -S(O)_{n^-}, -N(R_e)-, -C(O)-, -C(O)O-, -SO_2N(R_e)-, -C(O)O-, -SO_2N(R_e)-, -C(O)O-, -SO_2N(R_e)-, -C(O)O-, -SO_2N(R_e)-, -C(O)O-, -C(O)O-, -SO_2N(R_e)-, -C(O)O-, -C(O)O$
26	$-CON(R_e)$ -, $-N(R_e)CON(R_f)$ -, $-N(R_e)N(R_f)$ -, $-N(R_e)SO_2N(R_f)$ -, $-N(R_e)$ -O-, $=N$ -O-, lower
27	alkylene, perfluoro lower alkylene, polyfluoro lower alkylene, -O-lower alkylene,
28	$-S(O)_n$ -lower alkylene, $N(R_e)$ -lower alkylene, $-SO_2N(R_e)$ -lower alkylene, lower
29	alkylene- $SO_2N(R_e)$ -, - $CON(R_e)$ -lower alkylene, lower alkylene- $CON(R_e)$ -,
30	$-N(R_e)CON(R_f) - lower \ alkylene, \ lower \ alkylene - N(R_e)N(R_f) - , \ -N(R_e)SO_2N(R_f) - lower \ alkylene - N(R_e)N(R_f) - lower \ al$
31	alkylene, -N(R <sub>e</sub> )-O-lower alkylene, lower alkylene-N(R <sub>e</sub> )-O-, =N-O-lower alkylene,
32	lower heteroalkylene, -O-lower heteroalkylene, -S(O) $_{n}$ -lower heteroalkylene, N(R $_{e}$ )-lower
33	heteroalkylene, - $SO_2N(R_e)$ -lower heteroalkylene, lower heteroalkylene- $SO_2N(R_e)$ -,
34	$-CON(R_e) - lower \ heteroalkylene, \ lower \ heteroalkylene-CON(R_e) - , \ -N(R_e)CON(R_f) - lower$
35	heteroalkylene, lower heteroalkylene- $N(R_e)N(R_f)$ -, - $N(R_e)SO_2N(R_f)$ -lower
36	heteroalkylene, $-N(R_e)$ -O-lower heteroalkylene, lower heteroalkylene- $N(R_e)$ -O-,
37	=N-O-lower alkylene, aryl and heteroaryl, wherein R <sub>a</sub> , R <sub>b</sub> , R <sub>c</sub> , R <sub>d</sub> , R <sub>e</sub> and R <sub>f</sub> are each
38	members independently selected from the group consisting of H, lower alkyl, lower
39	heteroalkyl, -C(O)-lower alkyl, -C(O)-lower heteroalkyl, -S(O) $_2$ -lower alkyl, and -
40	S(O) <sub>2</sub> -lower heteroalkyl;
41	the subscript n is an integer of from 0 to 2;

the subscript m is an integer of from 0 to 3;

B is selected from the group consisting of:



with the proviso that when B is

wherein  $X^2$  is a substituted or unsubstituted member selected from the group consisting of a 5-6 membered cycloalkyl, 5-6 membered heterocycloalkyl containing from 1 to 3 heteroatoms, heteroaryl containing from 1 to 3 heteroatoms and aryl;

W is CH or N;

 $R_{\rm g} \ is \ selected \ from \ the \ group \ consisting \ of \ H, \ lower \ alkyl,$  lower alkoxy and F;

 $R_h$  is selected from the group consisting of H,  $-S(O)_n$ -lower alkyl,  $-S(O)_n$ -lower heteroalkyl,  $-S(O)_n$ -aryl and  $-S(O)_n$ -heteroaryl;

 $R_i$  is selected from the group consisting of H, lower alkyl, lower heteroalkyl, or a bond that links the atom bearing  $R_i$  with another atom in the  $X^2$  ring;

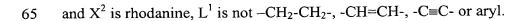
 $R_{j} \ is \ selected \ from \ the \ group \ consisting \ of \ H, \ lower \ alkyl, \ F$  and lower alkoxy; and

Hal is a halogen atom;

wherein when  $L^1$  and  $L^2$  may be linked together via a single bond, -O-, -S- or amide group to form a new 5 to 7 membered ring;

X<sup>2</sup>

 $B_a$ 



- 1 13. A compound in accordance with claim 12, wherein B is selected
- 2 from the group consisting of:

$$\begin{array}{c} X^4 \\ X^3 \\ X^5 \\ \end{array} \begin{array}{c} X^4 \\ X^5 \\ X^5 \\ X^5 \\ \end{array} \begin{array}{c} X^4 \\ X^5 \\$$

3

7

8

9

10

11

12

13

14

15

16

17

18

19

20

R<sub>k</sub> is selected from the group consisting of H, lower alkyl, lower heteroalkyl and F;

 $R_1$  is H or lower alkyl;

X<sup>3</sup> is selected from the group consisting of O, S, CH<sub>2</sub>, CH(lower alkyl), C(lower alkyl)<sub>2</sub>, NH and N(lower alkyl);

 $X^4$  is selected from the group consisting of O, S, NH and N(lower alkyl), or  $X^4$  and the carbon atom to which it is attached represents an sp<sup>3</sup>-hybridized carbon having two substituents independently selected from the group consisting of H, lower alkyl and lower heteroalkyl;

 $X^5$  is selected from the group consisting of O, S, NH and N(lower alkyl), or  $X^5$  and the carbon atom to which it is attached represents an sp<sup>3</sup>-hybridized carbon having two substituents independently selected from the group consisting of H, lower alkyl, lower alkoxy, aryloxy, lower thioalkoxy and arylthioxy; and

--- represents either a single or double bond, with the proviso that when a single bond is intended, the ring atom bearing said single bond bears an additional substituent selected from the group consisting of H, lower alkyl, lower alkoxy and F.

1 14. A compound of claim 13, wherein B is selected from the group 2 consisting of:

$$\begin{bmatrix} X^4 & X^3 & R_k \\ & & & \\$$

4 wherein

3

1415

1

2

3

4 5

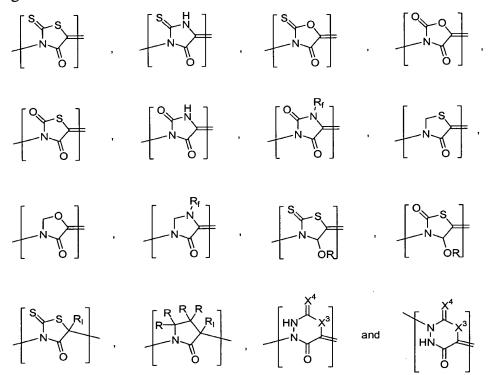
R<sub>k</sub>, R<sub>m</sub> and R<sub>n</sub> are each independently selected from the group consisting
of H, F, lower alkyl and lower alkoxy;

X<sup>3</sup> is selected from the group consisting of O, S, C(lower alkyl)<sub>2</sub>, NH and
N(lower alkyl);

X<sup>4</sup> is selected from the group consisting of O and S, or X<sup>4</sup> and the carbon
atom to which it is attached represents an sp<sup>3</sup>-hybridized carbon having two substituents
independently selected from the group consisting of H, lower alkyl and lower heteroalkyl;
X<sup>5</sup> is selected from the group consisting of O and S, or X<sup>5</sup> and the carbon

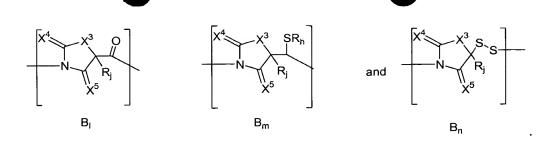
 $X^5$  is selected from the group consisting of O and S, or  $X^5$  and the carbon atom to which it is attached represents an sp<sup>3</sup>-hybridized carbon having two substituents independently selected from the group consisting of H, lower alkoxy and lower thioalkoxy.

15. A compound of claim 14, wherein B is selected from the group consisting of:



wherein any unlabeled R groups are independently selected from the group consisting of H, lower alkyl, lower alkoxy and F.

1 16. A compound of claim 12 wherein B is selected from the group 2 consisting of:



- 1 17. A compound of claim 12, wherein L<sup>1</sup> is selected from the group consisting of -N(R<sub>a</sub>)-, -N(R<sub>a</sub>)-alkylene, alkylene-SO<sub>2</sub>-N(R<sub>a</sub>)-, -SO<sub>2</sub>-N(R<sub>a</sub>)- and -N(R<sub>a</sub>)SO<sub>2</sub>-; and X<sup>1</sup> is selected from the group consisting of H, aryl and alkyl.
- 1 18. A compound of claim 12, wherein Ar<sup>1</sup> is selected from the group 2 consisting of substituted or unsubstituted biphenyl group, substituted or unsubstituted 3 bicyclic ring, substituted or unsubstituted phenyl group and substituted or unsubstituted 4 pyridyl.

1

19. A compound of claim 17, said compound having the formula:

2

wherein R<sub>p</sub> is selected from the group consisting of substituted or unsubstituted alkyl,

4 substituted or unsubstituted aryl and substituted or unsubstituted heteroaryl.

- 1
- 20. A compound of Claim 12, said compound having the formula (III):

2

3 wherein

4 the subscript q is an integer of from 0 to 4;

5	$R^1$ is hydrogen or a substituent having the formula $-L^1$ -COOH;
6	X is a moiety selected from $-S$ -, $-O$ -, and $-N(R_o)$ -, wherein $R_o$ is H or
7	lower alkyl;
8	R <sup>2</sup> is a substituted or unsubstituted aryl(C <sub>1</sub> -C <sub>8</sub> )alkyl, a substituted or
9	unsubstituted aryl( $C_1$ - $C_8$ )alkenyl, a substituted or unsubstituted aryl( $C_1$ - $C_8$ )alkynyl, a
10	substituted or unsubstituted alicyclic group having from 5-8 carbon atoms, or a group
11	having the formula $(R_{2a})_r$ - $(L)_s$ - $R_{2b}$ -, wherein $R_{2a}$ and $R_{2b}$ can be the same or different and
12	represent a substituted or unsubstituted heterocyclic group or a substituted or
13	unsubstituted phenyl group, R <sub>2a</sub> can also represent a substituted or unsubstituted
14	polycyclic group, and L represents a divalent linking group selected from methylene,
15	ethylene, propylene, -CH=CH-, -C=C-, -C(O)-, -O-, -S-, -S(O)-, -S(O) <sub>2</sub> -, or -N( $R_{2c}$ )-,
16	wherein $R_{2c}$ is selected from H or lower alkyl, and the subscripts r and s are each
17	independently 0 or 1;
18	R <sup>3</sup> is selected from the group consisting of H, substituted or unsubstituted
19	(C <sub>1</sub> -C <sub>8</sub> )alkyl, substituted and unsubstituted aryl or substituted and unsubstituted
20	heteroaryl;
21	Y represents O or S; and
22	Z represents O, S or $N(R_{2d})$ , wherein $R_{2d}$ is H or lower alkyl, or $R_{2d}$ and $R^1$
23	may be joined to form an imidazole or benzimidazole group;
24	with the proviso that when R <sup>1</sup> is hydrogen, R <sup>3</sup> is not substituted furan.

21. A compound of Claim 12, said compound having the formula (V):

3 wherein

1

2

4

7

8

9

 $R^1$  is H, -OH, -COOR<sub>u</sub>, -CONR<sub>v</sub>R<sub>w</sub>, -SO<sub>2</sub>NR<sub>x</sub>R<sub>y</sub> wherein R<sub>u</sub>, R<sub>v</sub>, R<sub>w</sub>, R<sub>x</sub>

and  $R_y$  are H or lower alkyl, or  $R^1$  is a mono-heterocyclic group selected from furan,

6 thiophene, pyridine, pyrimidine, pyridazine, 1,3-oxathiolane, tetrazole, oxadiazole,

oxazole, triazole, imidazoline, imidazole, thiazole, thiadiazole, pyrrole, piperidine,

morpholine, triazine and pyrazole; and

 $W_1$  and  $W_2$  are independently selected from H,  $(C_1-C_8)$ alkyl,  $(C_1-C_8)$ 

10 C<sub>8</sub>)alkenyl, (C<sub>1</sub>-C<sub>8</sub>)alkynyl, halogen, nitro, hydroxy, perfluoroalkyl, difluoromethyl, (C<sub>1</sub>-

- $C_8$ )alkoxy, phenoxy, phenyl( $C_1$ - $C_8$ )alkoxy, ( $C_1$ - $C_8$ )acyl, ( $C_1$ - $C_8$ )acyloxy, cyano,
- 12 carbalkoxy, thio, (C<sub>1</sub>-C<sub>8</sub>)alkylthio, (C<sub>1</sub>-C<sub>8</sub>)alkylsulfinyl, (C<sub>1</sub>-C<sub>8</sub>)alkylsulfonyl, amino, (C<sub>1</sub>-
- 13 C<sub>8</sub>)alkylamino, di(C<sub>1</sub>-C<sub>8</sub>)alkylamino, sulfonamido, carboxamido and (C<sub>1</sub>-
- 14 C<sub>8</sub>)alkanoylamino.
- 1 22. A compound of Claim 12, said compound having a formula
- 2 selected from the group consisting of

$$R^{2} \xrightarrow{N-N-S-O} \text{ and } R^{2} \xrightarrow{N-N-S-O} \text{ Alkyl}$$

R<sup>2</sup> is a substituted or unsubstituted mono- or bi-heterocyclic group, a substituted or unsubstituted polycyclic ring, a substituted or unsubstituted alicyclic group having 5-8 carbon atoms, a substituted or unsubstituted phenyl group, a substituted or unsubstituted biphenyl group, a substituted or unsubstituted phenylether group, a substituted or unsubstituted or unsubstituted stilbenyl group.

23. The compound of Claim 22, wherein said compound is selected from the group consisting of

$$CI$$
 $N-N-S$ 
 $CI$ 
 $N-N-S$ 
 $N-N-S$ 

24. A compound having the formula (VIIa):

$$R^{2} \xrightarrow{N-N-S} Ar^{1}$$

3	wherein
4	Ar <sup>1</sup> is selected from the group consisting of substituted or unsubstituted
5	aryl and substituted or unsubstituted heteroaryl;
6	X is selected from $-S$ -, $-O$ - and $-N(R_o)$ -, wherein $R_o$ is H or lower alkyl;
7	Y is O or S; and
8	Z is O, S or $N(R_{2d})$ , wherein $R_{2d}$ is H or lower alkyl, or $R_{2d}$ and $R^1$ may be
9	joined to form an imidazole or benzimidazole group; and
10	R <sup>2</sup> is a substituted or unsubstituted mono- or bi-heterocyclic group, a
11	substituted or unsubstituted polycyclic ring, a substituted or unsubstituted alicyclic group
12	having 5-8 carbon atoms, a substituted or unsubstituted phenyl group, a substituted or
13	unsubstituted biphenyl group, a substituted or unsubstituted phenylether group, a
14	substituted or unsubstituted cinnamenyl group, or a substituted or unsubstituted stilbenyl
15	group.

25. The compound of Claim 24, wherein said compound is selected from the group consisting of

26. A compound useful for the covalent modification of a viral RNA-dependent RNA polymerase (RdRp) protein, said compound having the formula:

 $X^{1}-L^{1}-X^{2}-A-L^{2}-Ar^{1}$ 

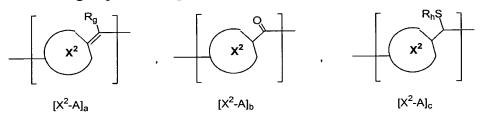
4 wherein

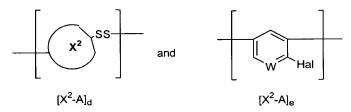
A is a electrophilic group that reacts with a cysteine residue of said viral RNA-dependent RNA polymerase protein;

Ar<sup>1</sup> is a member selected from the group consisting of substituted or unsubstituted aryl and substituted or unsubstituted heteroaryl;

9	X <sup>1</sup> is a member selected from the group consisting of -H, substituted or
10	unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted
11	heteroaryl, -CN, -CO <sub>2</sub> H, -SO <sub>3</sub> H, -C(O)NHOH, -NH <sub>2</sub> , -OH, -NH(lower alkyl), -O(lower
12	alkyl), -N(lower alkyl) <sub>2</sub> , and -C(O)-NH(3-tetrazolyl);
13	L1 is a divalent linking group selected from the group consisting of -O-,
14	$-S(O)_n-, -N(R_a)-, -C(O)-, -C(O)O-, -SO_2N(R_a)-, -CON(R_a)-, -N(R_a)CON(R_b)-, \\$
15	$-N(R_a)N(R_b)$ -, $-N(R_a)SO_2N(R_b)$ -, $-N(R_a)SO_2$ -, $-N(R_a)$ -O-, $=N$ -O-, lower alkylene,
16	-O-lower alkylene, -S(O) <sub>n</sub> -lower alkylene, N(R <sub>a</sub> )-lower alkylene, -SO <sub>2</sub> N(R <sub>a</sub> )-lower
17	alkylene, lower alkylene-SO <sub>2</sub> N(R <sub>a</sub> )-, -CON(R <sub>a</sub> )-lower alkylene, lower
18	alkylene- $CON(R_a)$ -, $-N(R_a)CON(R_b)$ -lower alkylene, lower alkylene- $N(R_a)N(R_b)$ -,
19	$-N(R_a)SO_2N(R_b)$ -lower alkylene, $-N(R_a)$ -O-lower alkylene, lower alkylene- $N(R_a)$ -O-,
20	=N-O-lower alkylene, lower heteroalkylene, -O-lower heteroalkylene, -S(O) <sub>n</sub> -lower
21	heteroalkylene, $N(R_a)$ -lower heteroalkylene, $-SO_2N(R_a)$ -lower heteroalkylene, lower
22	heteroalkylene- $SO_2N(R_a)$ -, - $CON(R_a)$ -lower heteroalkylene, lower
23	heteroalkylene- $CON(R_a)$ -, $-N(R_a)CON(R_b)$ -lower heteroalkylene, lower
24	heteroalkylene- $N(R_a)N(R_b)$ -, - $N(R_a)SO_2N(R_b)$ -lower heteroalkylene, - $N(R_a)$ -O-lower
25	heteroalkylene, lower heteroalkylene- $N(R_a)$ -O-, =N-O-lower alkylene and heteroaryl;
26	X <sup>2</sup> is a member selected from the group consisting of substituted or
27	unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted
28	cycloalkyl, and substituted or unsubstituted heterocycloalkyl;
29	L <sup>2</sup> is a divalent linking group selected from the group consisting of
30	$-CH_2CH_{2^-}, -(C(R_c)=C(R_d))_{m^-}, -O, -S(O)_{n^-}, -N(R_e), -C(O), -C(O)O, -SO_2N(R_e), -C(O), -C(O)$
31	$-CON(R_e)-, -N(R_e)CON(R_f)-, -N(R_e)N(R_f)-, -N(R_e)SO_2N(R_f)-, -N(R_e)-O-, =N-O-, \\ lower = -N(R_e)CON(R_f)-, -N(R_e)CON(R_f)-, -N(R_e)N(R_f)-, -N(R_e)SO_2N(R_f)-, \\ -N(R_e)SO_2N(R_f)-, -N(R_e)SO_2N(R_f)-, -N(R_e)SO_2N(R_f)-, -N(R_e)SO_2N(R_f)-, \\ -N(R_e)SO_2N(R_f)-, -N(R_e)SO_2N(R_f)-, -N(R_e)SO_2N(R_f)-, \\ -N(R_e)SO_2N(R_f)-, -N(R_e)SO_2N(R_f)-, -N(R_e)SO_2N(R_f)-, \\ -N(R_e)SO_2N(R_f)-, -N(R_e)SO_2N(R_f)-, -N(R_e)SO_2N(R_f)-, \\ -N(R_e)SO_2N($
32	alkylene, perfluoro lower alkylene, polyfluoro lower alkylene, -O-lower alkylene,
33	$-S(O)_n$ -lower alkylene, $N(R_e)$ -lower alkylene, $-SO_2N(R_e)$ -lower alkylene, lower
34	alkylene-SO <sub>2</sub> N(R <sub>e</sub> )-, -CON(R <sub>e</sub> )-lower alkylene, lower alkylene-CON(R <sub>e</sub> )-,
35	$-N(R_e)CON(R_f)-lower\ alkylene,\ lower\ alkylene-N(R_e)N(R_f)-,\ -N(R_e)SO_2N(R_f)-lower$
36	alkylene, - $N(R_e)$ -O-lower alkylene, lower alkylene- $N(R_c)$ -O-, = $N$ -O-lower alkylene,
37	lower heteroalkylene, -O-lower heteroalkylene, - $S(O)_n$ -lower heteroalkylene, $N(R_e)$ -lower
38	heteroalkylene, $-SO_2N(R_e)$ -lower heteroalkylene, lower heteroalkylene- $SO_2N(R_e)$ -,
39	$-CON(R_e) - lower \ heteroalkylene, \ lower \ heteroalkylene-CON(R_e) - , \ -N(R_e)CON(R_f) - lower$
40	heteroalkylene, lower heteroalkylene- $N(R_e)N(R_f)$ -, - $N(R_e)SO_2N(R_f)$ -lower
41	heteroalkylene, -N(R <sub>e</sub> )-O-lower heteroalkylene, lower heteroalkylene-N(R <sub>e</sub> )-O-,
42	=N-O-lower alkylene, aryl and heteroaryl;

- wherein R<sub>a</sub>, R<sub>b</sub>, R<sub>c</sub>, R<sub>d</sub>, R<sub>e</sub> and R<sub>f</sub> are each members independently selected from the group consisting of H, lower alkyl, lower heteroalkyl, -C(O)-lower alkyl, -C(O)-lower heteroalkyl,  $-S(O)_2$ -lower alkyl, and  $-S(O)_2$ -lower heteroalkyl; the subscript n is an integer of from 0 to 2; the subscript m is an integer of from 0 to 3; the bond between X<sup>2</sup> and A can be a single, double or triple bond, depending on the nature of X<sup>2</sup> and A; and wherein when L<sup>1</sup> and L<sup>2</sup> may be linked together via a single bond, -O-, -S-or amide group to form a new 5 to 7 membered ring.
  - 27. A compound in accordance with claim 26, wherein  $X^2$  is selected from the group consisting of a 5 to 7 membered cycloalkyl ring, a 5 to 7 membered heterocycloalkyl ring containing from 1 to 3 heteroatoms, an aryl group and a heteroaryl group; A is selected from the group consisting of an sp<sup>2</sup>-hybridized carbon atom and an sp<sup>3</sup>-hybridized carbon atom;  $L^2$  is a single bond; and  $X^2$  and A are joined *via* a single or double bond.
  - 28. A compound in accordance with claim 27, wherein  $-X^2$ -A- is selected from the group consisting of:

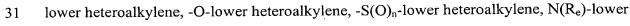




wherein  $R_g$  is selected from the group consisting of H, lower alkyl, lower salkoxy and F;

 $R_h$  is selected from the group consisting of H,  $-S(O)_n$ -lower alkyl,  $-S(O)_n$ -lower heteroalkyl,  $-S(O)_n$ -aryl and  $-S(O)_n$ -heteroaryl; W is CH or N; Hal is a halogen atom; and  $X^2$  is a substituted or unsubstituted member selected from the group consisting

- 9 of a 5-6 membered cycloalkyl, 5-6 membered heterocycloalkyl containing from 1 to 3
- heteroatoms, heteroaryl containing from 1 to 3 heteroatoms and aryl.
- 1 29. A compound having the formula (II):
- $X^{1}-L^{1}-B-L^{2}-Ar^{1}$
- 3 wherein
- 4 Ar<sup>1</sup> is a member selected from the group consisting of substituted or
- 5 unsubstituted aryl and substituted or unsubstituted heteroaryl;
- $X^1$  is a member selected from the group consisting of -H, substituted or
- 7 unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted
- 8 heteroaryl, -CN, -CO<sub>2</sub>H, -SO<sub>3</sub>H, -C(O)NHOH, -NH<sub>2</sub>, -OH, -NH(lower alkyl), -O(lower
- 9 alkyl), -N(lower alkyl)<sub>2</sub>, and -C(O)-NH(3-tetrazolyl);
- 10 L<sup>1</sup> is a divalent linking group selected from the group consisting of -O-,
- 11  $-S(O)_n$ ,  $-N(R_a)$ , -C(O), -C(O)O,  $-SO_2N(R_a)$ ,  $-CON(R_a)$ ,  $-N(R_a)CON(R_b)$ ,
- $-N(R_a)N(R_b)$ -,  $-N(R_a)SO_2N(R_b)$ -,  $-N(R_a)SO_2$ -,  $-N(R_a)-O$ -, =N-O-, lower alkylene,
- -O-lower alkylene, -S(O)<sub>n</sub>-lower alkylene, N(R<sub>a</sub>)-lower alkylene, -SO<sub>2</sub>N(R<sub>a</sub>)-lower
- alkylene, lower alkylene-SO<sub>2</sub>N(R<sub>a</sub>)-, -CON(R<sub>a</sub>)-lower alkylene, lower
- alkylene- $CON(R_a)$ -,  $-N(R_a)CON(R_b)$ -lower alkylene, lower alkylene- $N(R_a)N(R_b)$ -,
- -N(R<sub>a</sub>)SO<sub>2</sub>N(R<sub>b</sub>)-lower alkylene, -N(R<sub>a</sub>)-O-lower alkylene, lower alkylene-N(R<sub>a</sub>)-O-,
- 17 =N-O-lower alkylene, lower heteroalkylene, -O-lower heteroalkylene, -S(O)<sub>n</sub>-lower
- heteroalkylene, N(R<sub>a</sub>)-lower heteroalkylene, -SO<sub>2</sub>N(R<sub>a</sub>)-lower heteroalkylene, lower
- 19 heteroalkylene-SO<sub>2</sub>N(R<sub>a</sub>)-, -CON(R<sub>a</sub>)-lower heteroalkylene, lower
- 20 heteroalkylene-CON(R<sub>a</sub>)-, -N(R<sub>a</sub>)CON(R<sub>b</sub>)-lower heteroalkylene, lower
- heteroalkylene- $N(R_a)N(R_b)$ -,  $-N(R_a)SO_2N(R_b)$ -lower heteroalkylene,  $-N(R_a)$ -O-lower
- 22 heteroalkylene, lower heteroalkylene-N(R<sub>a</sub>)-O-, =N-O-lower alkylene and heteroaryl;
- L<sup>2</sup> is a divalent linking group selected from the group consisting of
- 24  $-CH_2CH_2$ ,  $-(C(R_c)=C(R_d))_m$ ,  $-O_2$ ,  $-S(O)_n$ ,  $-N(R_e)$ , -C(O),  $-C(O)O_2$ ,  $-SO_2N(R_e)$ ,
- 25  $-CON(R_e)$ -,  $-N(R_e)CON(R_f)$ -,  $-N(R_e)N(R_f)$ -,  $-N(R_e)SO_2N(R_f)$ -,  $-N(R_e)$ -O-, =N-O-, lower
- alkylene, perfluoro lower alkylene, polyfluoro lower alkylene, -O-lower alkylene,
- 27 -S(O)<sub>n</sub>-lower alkylene, N(R<sub>e</sub>)-lower alkylene, -SO<sub>2</sub>N(R<sub>e</sub>)-lower alkylene, lower
- 28 alkylene-SO<sub>2</sub>N(R<sub>e</sub>)-, -CON(R<sub>e</sub>)-lower alkylene, lower alkylene-CON(R<sub>e</sub>)-,
- 29  $-N(R_e)CON(R_f)$ -lower alkylene, lower alkylene- $N(R_e)N(R_f)$ -,  $-N(R_e)SO_2N(R_f)$ -lower
- 30 alkylene, -N(R<sub>e</sub>)-O-lower alkylene, lower alkylene-N(R<sub>e</sub>)-O-, =N-O-lower alkylene,



- 32 heteroalkylene, -SO<sub>2</sub>N(R<sub>e</sub>)-lower heteroalkylene, lower heteroalkylene-SO<sub>2</sub>N(R<sub>e</sub>)-,
- -CON(R<sub>e</sub>)-lower heteroalkylene, lower heteroalkylene-CON(R<sub>e</sub>)-, -N(R<sub>e</sub>)CON(R<sub>f</sub>)-lower
- 34 heteroalkylene, lower heteroalkylene-N(R<sub>e</sub>)N(R<sub>f</sub>)-, -N(R<sub>e</sub>)SO<sub>2</sub>N(R<sub>f</sub>)-lower
- 35 heteroalkylene,  $-N(R_e)$ -O-lower heteroalkylene, lower heteroalkylene- $N(R_e)$ -O-,
- 36 =N-O-lower alkylene, aryl and heteroaryl;
- wherein R<sub>a</sub>, R<sub>b</sub>, R<sub>c</sub>, R<sub>d</sub>, R<sub>e</sub> and R<sub>f</sub> are each members independently selected
- from the group consisting of H, lower alkyl, lower heteroalkyl, -C(O)-lower alkyl,
- -C(O)-lower heteroalkyl,  $-S(O)_2$ -lower alkyl, and  $-S(O)_2$ -lower heteroalkyl;
- the subscript n is an integer of from 0 to 2;
- 41 the subscript m is an integer of from 0 to 3;
- B is selected from the group consisting of:

$$\begin{bmatrix} x^2 \\ B_a \end{bmatrix} \qquad \begin{bmatrix} x^2 \\ B_b \end{bmatrix} \qquad \begin{bmatrix} x^2 \\ B_c \end{bmatrix}$$

43

 $X^2$  is a substituted or unsubstituted member selected from the group

46 consisting of a 5-6 membered cycloalkyl, 5-6 membered heterocycloalkyl containing

from 1 to 3 heteroatoms, heteroaryl containing from 1 to 3 heteroatoms and aryl;

48 W is CH or N;

49 R<sub>g</sub> is selected from the group consisting of H, lower alkyl, lower alkoxy

50 and F;

53

 $R_h$  is selected from the group consisting of H,  $-S(O)_n$ -lower alkyl,  $-S(O)_n$ -

lower heteroalkyl,  $-S(O)_n$ -aryl and  $-S(O)_n$ -heteroaryl;

R<sub>i</sub> is selected from the group consisting of H, lower alkyl, lower

heteroalkyl, or a bond that links the atom bearing  $R_i$  with another atom in the  $X^2$  ring;

- R<sub>j</sub> is selected from the group consisting of H, lower alkyl, F and lower alkoxy; and Hal is a halogen atom; wherein when L<sup>1</sup> and L<sup>2</sup> may be linked together *via* a single bond, -O-, -Sor amide group to form a new 5 to 7 membered ring.
- 1 30. A compound in accordance with claim 29, wherein B is selected 2 from the group consisting of:

$$\begin{bmatrix} X^4 & X^3 & R_k \\ X^5 & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ &$$

3

4

5 6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

 $R_k$  is selected from the group consisting of H, lower alkyl, lower heteroalkyl and F;

R<sub>1</sub> is H or lower alkyl;

X<sup>3</sup> is selected from the group consisting of O, S, CH<sub>2</sub>, CH(lower alkyl), C(lower alkyl)<sub>2</sub>, NH and N(lower alkyl);

 $X^4$  is selected from the group consisting of O, S, NH and N(lower alkyl), or  $X^4$  and the carbon atom to which it is attached represents an sp<sup>3</sup>-hybridized carbon having two substituents independently selected from the group consisting of H, lower alkyl and lower heteroalkyl; and

X<sup>5</sup> is selected from the group consisting of O, S, NH and N(lower alkyl), or X<sup>5</sup> and the carbon atom to which it is attached represents an sp<sup>3</sup>-hybridized carbon having two substituents independently selected from the group consisting of H, lower alkyl, lower alkoxy, aryloxy, lower thioalkoxy and arylthioxy; and --- represents either a single or double bond, with the proviso that when a single bond is intended, the ring atom bearing said single bond bears an additional substituent selected from the group consisting of H, lower alkyl, lower alkoxy and F.

1 31. A compound of claim 30, wherein B is selected from the group 2 consisting of:

$$\begin{bmatrix} X^4 & X^3 & R_k \\ & & & \\$$

wherein  $R_k$ ,  $R_m$  and  $R_n$  are each independently selected from the group consisting of H, F, lower alkyl and lower alkoxy;  $X^3$  is selected from the group consisting of O, S, C(lower alkyl)<sub>2</sub>, NH and N(lower alkyl);  $X^4$  is selected from the group consisting of O, S, or  $X^4$  and the carbon atom to which it is attached represents an sp<sup>3</sup>-hybridized carbon having two substituents independently selected from the group consisting of H, lower alkyl and lower heteroalkyl;  $X^5$  is selected from the group consisting of O, S, or  $X^5$  and the carbon atom to which it is attached represents an sp<sup>3</sup>-hybridized carbon having two substituents independently selected from the group consisting of H, lower alkoxy and lower thioalkoxy.

32. A compound of claim 31, wherein B is selected from the group

consisting of:

4 wherein any unlabeled R groups are independently selected from the group consisting of

5 H, lower alkyl, lower alkoxy and F.

1 33. A compound of claim 29, wherein B is selected from the group

2 consisting of:

3

1

2

3 4

1

2

4 1 2

$$\begin{bmatrix} X^4 & X^3 & 0 \\ & & & \\ &$$

1 34. A compound of claim 29 wherein L<sup>1</sup> is selected from the group

2 consisting of  $-N(R_a)$ -,  $-N(R_a)$ -alkylene, alkylene- $SO_2$ - $N(R_a)$ -,  $-SO_2$ - $N(R_a)$ - and

3  $-N(R_a)SO_2$ ; and  $X^1$  is selected from the group consisting of H, aryl and alkyl.

35. A compound of claim 29, wherein Ar<sup>1</sup> is selected from the group consisting of substituted or unsubstituted biphenyl group, substituted or unsubstituted bicyclic ring, substituted or unsubstituted phenyl group and substituted or unsubstituted pyridyl.

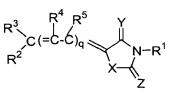
36. A compound of claim 34, said compound having the formula:

wherein  $R_p$  is a member selected from the group consisting of substituted or unsubstituted alkyl, substituted or unsubstituted aryl and substituted or unsubstituted heteroaryl.

37. A compound of Claim 29, said compound having the formula (III):

1

2



34 wherein

5 the subscript q is an integer of from 0 to 4;

6 R<sup>1</sup> is hydrogen or a substituent having the formula –L<sup>1</sup>-COOH;

7 X is a moiety selected from -S-, -O-, and  $-N(R_o)$ -, wherein  $R_o$  is H or

8 lower alkyl;

 $R^2$  is a substituted or unsubstituted aryl( $C_1$ - $C_8$ )alkyl, a substituted or

unsubstituted aryl(C<sub>1</sub>-C<sub>8</sub>)alkenyl, a substituted or unsubstituted aryl(C<sub>1</sub>-C<sub>8</sub>)alkynyl, a

substituted or unsubstituted alicyclic group having from 5-8 carbon atoms, or a group

having the formula  $(R_{2a})_r$ - $(L)_s$ - $R_{2b}$ -, wherein  $R_{2a}$  and  $R_{2b}$  can be the same or different and

13 represent a substituted or unsubstituted heterocyclic group or a substituted or

unsubstituted phenyl group, R<sub>2a</sub> can also represent a substituted or unsubstituted

polycyclic group, and L represents a divalent linking group selected from methylene,

16 ethylene, propylene, -CH=CH-, -C $\equiv$ C-, -C(O)-, -O-, -S-, -S(O)-, -S(O)<sub>2</sub>-, or -N(R<sub>2c</sub>)-,

wherein R<sub>2c</sub> is selected from H or lower alkyl, and the subscripts r and s are each

independently 0 or 1;

Y represents O or S; and

Z represents O, S or  $N(R_{2d})$ , wherein  $R_{2d}$  is H or lower alkyl, or  $R_{2d}$  and  $R^1$ 

21 may be joined to form an imidazole or benzimidazole group;

with the proviso that when  $R^1$  is hydrogen  $R^2$  is not substituted or unsubstituted furan.

38. A compound of Claim 29, said compound having the formula (V):

$$R^{3} = R^{4} R^{5}$$

$$R^{2} = C - C)_{q}$$

$$X = V_{1}$$

$$X = V_{2}$$

$$X = V_{2}$$

$$V_{1} = V_{2}$$

$$V_{2} = V_{3}$$

3 wherein

4 R<sup>1</sup> is H, -OH, -COOR<sub>u</sub>, -CONR<sub>v</sub>R<sub>w</sub>, -SO<sub>2</sub>NR<sub>x</sub>R<sub>y</sub> wherein R<sub>u</sub>, R<sub>v</sub>, R<sub>w</sub>, R<sub>x</sub>

5 and R<sub>v</sub> are H or lower alkyl, or R<sup>1</sup> is a mono-heterocyclic group selected from furan,

6 thiophene, pyridine, pyrimidine, pyridazine, 1,3-oxathiolane, tetrazole, oxadiazole,

7 oxazole, triazole, imidazoline, imidazole, thiazole, thiadiazole, pyrrole, piperidine,

8 morpholine, triazine and pyrazole; and

W<sub>1</sub> and W<sub>2</sub> are independently selected from H, (C<sub>1</sub>-C<sub>8</sub>)alkyl, (C<sub>1</sub>-C<sub>8</sub>)alkynyl, halogen, nitro, hydroxy, perfluoroalkyl, difluoromethyl, (C<sub>1</sub>-C<sub>8</sub>)alkoxy, phenoxy, phenyl(C<sub>1</sub>-C<sub>8</sub>)alkoxy, (C<sub>1</sub>-C<sub>8</sub>)acyl, (C<sub>1</sub>-C<sub>8</sub>)acyloxy, cyano, carbalkoxy, thio, (C<sub>1</sub>-C<sub>8</sub>)alkylthio, (C<sub>1</sub>-C<sub>8</sub>)alkylsulfinyl, (C<sub>1</sub>-C<sub>8</sub>)alkylsulfonyl, amino, (C<sub>1</sub>-C<sub>8</sub>)alkylamino, di(C<sub>1</sub>-C<sub>8</sub>)alkylamino, sulfonamido, carboxamido and (C<sub>1</sub>-C<sub>8</sub>)alkanoylamino.

1 39. A compound of Claim 29, said compound having a formula 2 selected from the group consisting of

$$R^{2} \xrightarrow{N-N-S} Ar^{1} \qquad \text{and} \qquad R^{2} \xrightarrow{N-N-S} Alkyl$$

4 wherein

R<sup>2</sup> is a substituted or unsubstituted mono- or bi-heterocyclic group, a substituted or unsubstituted polycyclic ring, a substituted or unsubstituted alicyclic group having 5-8 carbon atoms, a substituted or unsubstituted phenyl group, a substituted or unsubstituted biphenyl group, a substituted or unsubstituted phenylether group, a substituted or unsubstituted or unsubstituted stilbenyl group.

. A compound having the formula:

3 wherein

X is a member selected from the group consisting of O, S, NR<sup>11</sup> and CR<sup>11</sup>R<sup>12</sup> wherein R<sup>11</sup> and R<sup>12</sup> are each members independently selected from the group consisting of H, substituted or unsubstituted (C<sub>1</sub>-C<sub>8</sub>)alkyl, substituted or unsubstituted (C<sub>1</sub>-C<sub>8</sub>)alkoxy and substituted or unsubstituted (C<sub>1</sub>-C<sub>8</sub>)acyl;

Y is a member selected from the group consisting of O and S, or taken

Y is a member selected from the group consisting of O and S, or taken together with the carbon atom to which it is attached forms a methylene group;

 $Z^1$  and  $Z^2$  are each members independently selected from the group consisting of H and substituted or unsubstituted (C<sub>1</sub>-C<sub>8</sub>)alkoxy, or taken together form an oxo moiety;

13	R <sup>1</sup> is a member selected from the group consisting of substituted or
14	unsubstituted ( $C_1$ - $C_8$ )alkyl, substituted or unsubstituted ( $C_1$ - $C_8$ )alkylamino, substituted or
15	unsubstituted di(C1-C8)alkylamino, substituted or unsubstituted (C1-C8)acylamino, amino
16	H, substituted or unsubstituted aryl(C <sub>1</sub> -C <sub>8</sub> )alkyl, substituted or unsubstituted
17	heteroaryl(C <sub>1</sub> -C <sub>8</sub> )alkyl, substituted or unsubstituted heterocycloalkyl and -NHSO <sub>2</sub> -Ar <sup>1</sup> ,
18	wherein Ar1 is selected from the group consisting of substituted or unsubstituted aryl and
19	substituted or unsubstituted heteroaryl; and
20	R <sup>2</sup> and R <sup>3</sup> are each members independently selected from the group
21	consisting of halo, substituted or unsubstituted (C1-C8)alkyl and substituted or
22	unsubstituted (C <sub>1</sub> -C <sub>8</sub> )acyl, or taken together form a group of the formula:

<sup>R⁴</sup> <sub>7√</sub> <sub>7</sub>5

2324

25

26

27

28

wherein  $R^4$  and  $R^5$  are each members independently selected from the group consisting of H, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl, with the proviso that no more than one of  $R^4$  and  $R^5$  are H; with the proviso that when  $Z^1$  and  $Z^2$  taken together form an oxo moiety and  $R^2$  and  $R^3$  taken together form a group of the formula:

R<sup>4</sup> R<sup>5</sup>

2930

R<sup>1</sup> is not substituted or unsubstituted (C<sub>1</sub>-C<sub>8</sub>)alkyl or H

- 1 41. A compound in accordance with claim 40, wherein R<sup>1</sup> is selected 2 from the group consisting of amino and substituted or unsubstituted -NHSO<sub>2</sub>-Ar<sup>1</sup>.
- 1 42. A compound in accordance with claim 40, wherein  $Z^1$  and  $Z^2$  taken 2 together are oxo.
- 1 43. A compound in accordance with claim 40, wherein Y is O or S and  $Z^1$  and  $Z^2$  taken together are oxo.
- 1 44. A compound in accordance with claim 40, wherein X and Y are S and Z<sup>1</sup> and Z<sup>2</sup> taken together are oxo.
- 1 45. A compound in accordance with claim 40, wherein R<sup>1</sup> is selected 2 from the group consisting of substituted or unsubstituted (C<sub>1</sub>-C<sub>8</sub>)alkylamino, substituted

- or unsubstituted di(C<sub>1</sub>-C<sub>8</sub>)alkylamino, substituted or unsubstituted (C<sub>1</sub>-C<sub>8</sub>)acylamino, amino, and -NHSO<sub>2</sub>-Ar<sup>1</sup>, wherein Ar<sup>1</sup> is selected from the group consisting of substituted or unsubstituted aryl and substituted or unsubstituted heteroaryl; X and Y are each
- 6 independently selected from the group consisting of O and S; Z<sup>1</sup> and Z<sup>2</sup> taken together are 7 oxo; and R<sup>2</sup> and R<sup>3</sup> taken together are a group having the formula:

R<sup>4</sup> R<sup>5</sup>

8

10

11

1 2

1

comprising

wherein R<sup>4</sup> and R<sup>5</sup> are each members independently selected from the group consisting of H, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl, with the proviso that only one of R<sup>4</sup> and R<sup>5</sup> is H.

46. A pharmaceutical composition, comprising a pharmaceutically acceptable carrier and a therapeutically or prophylactically effective amount of a compound of any one of claims 1, 9, 12, 24, 26, 29 and 40.

47. A method for the treatment or prevention of a viral infection,

administering to a subject suffering from or at risk for said viral infection an effective amount of a compound of any one of claims 1, 9, 12, 24, 26, 29 and 40.

- 1 48. The method of Claim 47, wherein said viral infection is hepatitis C virus infection.
- 1 49. The method of Claim 47, wherein said compound is administered 2 in combination with a therapeutically effective amount of an antiviral agent.
- 1 50. The method of Claim 49, wherein said antiviral agent is an 2 interferon.
- 51. A method for treating or preventing a viral infection, comprising administering to a subject in head thereof a therapeutically effective amount of a compound that binds to a cysteine residue in the RNA-dependent RNA polymerase (RdRp) protein of a virus forming a covalent bond.
  - 52. The method of plaim 51, wherein said RdRp protein is NS5B.

1	53. The method of Claim 51, wherein said viral infection is hepat	itis (
2	virus infection.	
1	54. The method of Claim 51, wherein said compound comprises a	ın
2	electrophilic group that reacts with a cysteine residue of said RdRp protein.	
1	55. The method of Claim 54, wherein said electrophilic group is	
2	selected from the group consisting of an activated double or triple bond, an electroph	nilic
3	center, a carboxylic acid or carboxylic acid derivative, a sulfur-containing group and	l an
4	activated or unactivated carbonyl group.	